

JAPANESE MEDICAL MATERIAL

A-392

AKTCOR

(Tyramine and Tyramine Methyl Ether Hydrochlorides)

291779

Medical No. 222

18 May 1946

MEDICAL ANALYSIS SECTION
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Aktcor

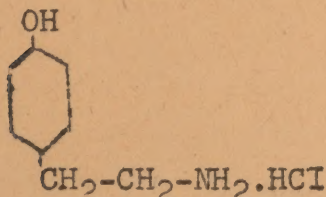
(Tyramine and Tyramine Methyl Ether Hydrochlorides)

SOURCE: Tokyo, Japan.IMPORTANCE: Not previously reported. A cardiac and circulatory stimulant preparation for oral and hypodermic use. No identical product is listed in available standard American references.DESCRIPTION:

Per-oral Solution: A slightly turbid solution of 100 cc in a 4 oz. amber bottle which is enclosed in a cardboard box.

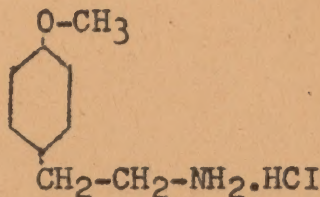
Ampoules: A slightly turbid liquid of 1.1 cc in ampoules packaged five per cardboard box. A residue is apparent in each ampoule.

SUMMARY OF GENERAL INFORMATION: Aktcor is an aqueous solution containing TYRAMINE (2%) and TYRAMINE METHYL ETHER (1%) in the form of their hydrochloride salts. Their chemical Structures follow:



TYRAMINE HYDROCHLORIDE

(p-Oxyphenyl-Ethylamine Hydrochloride)



METHYL ETHER

of Tyramine Hydrochloride

It is available as a per-oral solution and in the form of

ampoules.

The stimulant effects of Aktcor are due to the synergistic action of its constituents. Its action is due to selective stimulation of the respiratory center and heart. Effects are observable within 5 to 15 minutes after injection and last for about 3 hours. No complications result.

The action and uses of tyramine are well described in American literature. However, no similar information is available on the methyl ether of tyramine, whose effects (especially respiratory stimulation) are claimed to be greater and of longer duration than tyramine or lobeline. The ether is also claimed to be less toxic than lobeling.

A translation of the literature enclosed with Aktcor is part of this report and includes its properties, pharmacological action, clinical results, use in prescriptions, directions for use and dosage, packaging and price, and manufacturer.

PHOTOGRAPHS: Figure 1 - Package and bottle of Aktcor Liquor
Figure 2 - Closed package of Aktcor Ampoules
Figure 3 - Open package of Aktcor Ampoules
Figure 4 - Aktcor literature

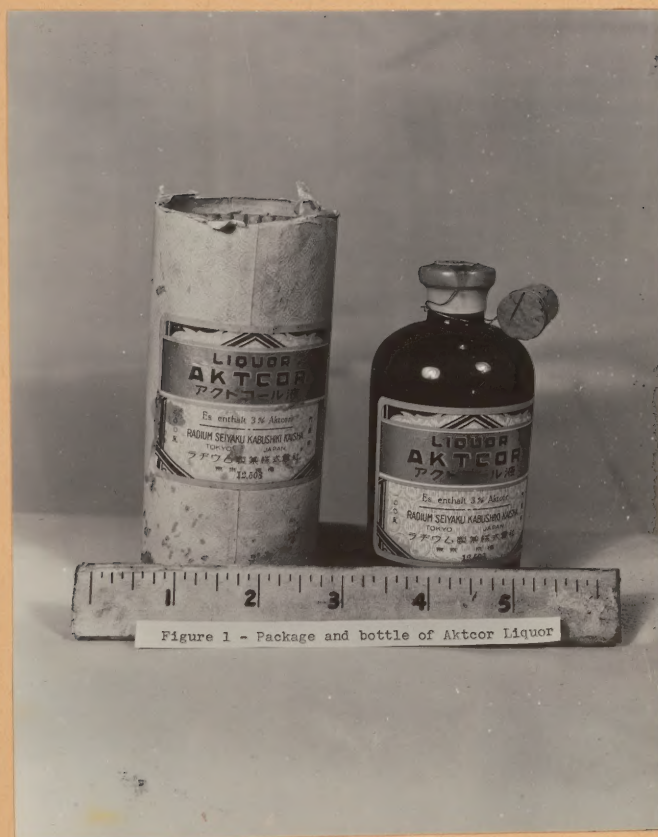
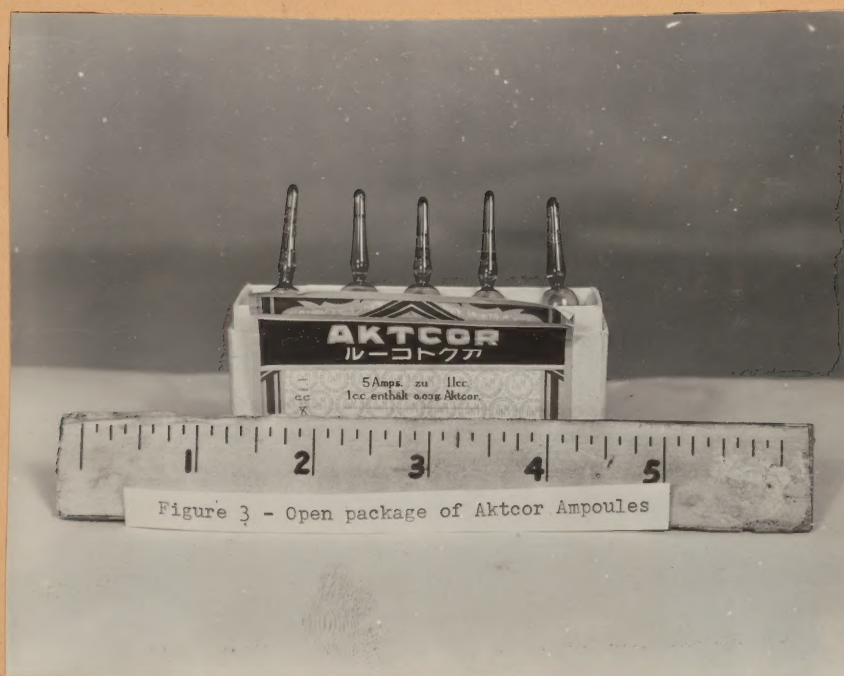
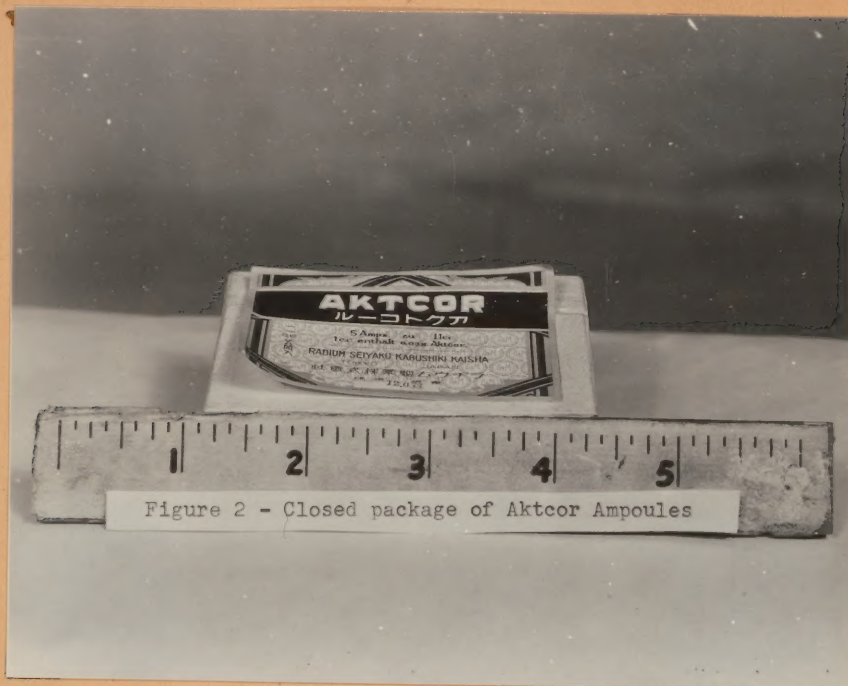


Figure 1 - Package and bottle of Aktcor Liquor



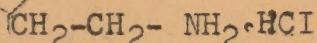
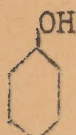
Translation of Literature with Aktcor

AKTCOR

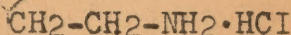
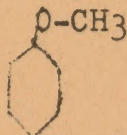
A synthetic water-soluble cardiac and respiratory stimulant, discovered by Doctor of Pharmacy Ryu Kondo.

PROPERTIES: Aktcor is a water-soluble stimulant consisting of Tyramine (2%) and Tyramine Methyl Ether (1%), manufactured by synthesis. It has a cardiac stimulatory effect excelling Camphor, as well as other prominent effects such as the stimulation of respiration and excretion of urine. It is rapidly absorbed and its effects are positive and lasting. Compared with Adrenalin, its effects last longer and there are no complications. Aktcor is prepared as a solution for oral use and as ampoules for injection.

Chemically, Aktcor consists of the following compounds:



Tyramine Hydrochloride
(p-Oxyphenyl-Ethylamine
Hydrochloride)



Methyl Ether of
Tyramine Hydrochloride

PHARMACOLOGICAL ACTION: The following is a summary of the results of medical experiments conducted with this drug by Dr. Kure.

1. Tyramine has powerful and positive effects, stimulating the heart and respiratory center as well as stimulating the excretion of urine. It enlarges the capillary bronchi, thereby increasing, instead of decreasing, respirations, and by increasing further the length of each respiration it improves the blood circulation, eases the difficulty of breathing, pains in the chest, etc., which are due to the obstruction of blood circulation, stricture of the heart, asthma and other diseases. It exhilarates the patient and improves his condition. It increases blood pressure moderately and therefore is effective in the prevention and treatment of fainting.

2. Tyramine Methyl Ether has a stronger and more durable action than Tyramine, especially its stimulatory effect on the respiratory center. Compared with Lobeline, it is less toxic, yet has a greater stimulating effect on the heart and respiration. Aktcor is superior to Coramine and Ephedrine as a respiratory stimulant. Ephedrine, moreover, seems to have a somewhat stronger paralyzing effect on the nerve center.

In short, because of synergistic action, it can be said that Aktcor is an ideal stimulant possessing both a cardiac stimulant effect superior to Digitales or Camphor and a respiratory stimulant effect excelling Lobeline. Since Aktcor is a synthetic, its action is lasting and constant.

The activity of Aktcor as a respiratory stimulant is due, in all probability, to the following two actions:

1. By stimulating the respiratory center selectively and, at the same time, by irritating the peripheral sympathetic nerve, it enlarges the bronchi and accordingly makes respirations deeper and decreases them in number.

2. Cardiac stimulation and moderate elevation of blood pressure improves blood circulation and, concurrent with removing the abnormal irritation of the respiratory center, brings on a gain in the central energy of the patient, due to the recovery of nourishment.

CLINICAL RESULTS:

1. Doctor of Medicine Hyakuta Tsushimo experimented with Aktcor on 24 patients with varying ailments, such as nephritis, pneumonia, dilatation of the aorta, myocarditis, bronchial asthma, cardiac failure, adhesive pericarditis, atrophy of the kidney, beriberi, etc., and reported that from 10 to 15 minutes after its injection the patient's respirations and pulse decreased. Relief from difficulty in breathing was effected for a period in excess of three hours in satisfactory cases.

2. Doctor of Medicine Saburo Kawamura of the Yokohama Doai Kinen (Fellowship Commemoration) Hospital experimented with Aktcor on patients with the following ailments; cardiac failure, general cardiac disorders, namely dropsy, respiratory difficulty accompanied by pains in the chest, hypertension, bronchial asthma, dysentery-like disease with symptoms of acute faintness of the heart and paralyzes of the blood vessels, dyspnea, congenital cardiac deformities resulting in faintness of the heart and pneumonia accompanied with difficulty in respiration. In each case, 5 to 10 minutes after its injection, elevation in blood pressure, decrease in number of respirations, strengthening of the heart beat, and a stronger pulse were observed. The patient was relieved from pains in the chest, could breathe easily and felt quite exhilarated. Administered successively several times a day, Aktcor stimulates not only cardiac action but also the excretion of urine.

3. According to experiments made by Yasuyuki Wakazono, M.B. of the Showa Medical College, in cases of respiratory difficulty, Aktcor decreases the number of respirations, promotes full normal breathing, and at the same time raises blood pressure and stimulates cardiac action and pulsation. The solubility of Aktcor in water results in rapid absorption, rapid effects, lack of pain and lack of induration. Physiological effects are noted within 5 minutes after injection and remain for many hours.

4. Doctor of Medicine Masato Endo states, "During several cases of surgery it was applied to patients with respiratory difficulty, collapse, etc., and in each case Aktcor proved comparable to Lobeline and Coramine. It produced no toxic reactions. It is also more economical to use than foreign preparations.

5. Major Hideo Shimizu, Army Surgeon, injected Aktcor as a first-aid measure in patients who fainted because of cerebral anemia, accidental injuries and Calmotin and Adalin poisoning (with suicidal intent). All the patients were treated successfully. He further recommended that Aktcor could be used to advantage as a cardiac and respiratory stimulant in cases of gas asphyxiation.

6. Doctor of Medicine Reizo Yoshida of the Manchi Hospital (for Infections Diseases), sponsored by the city of Yokohama, administered to patients with typhoid fever, diphtheria, scarlet fever and pleurisy, 5 cc of Aktcor per day continuously, and as a result prevented weakness of the heart, stimulated its action, increased the blood pressure, effected normal respiration and increased urinary output without any accompanying toxic reactions.

INDICATIONS: Aktcor is effective for treatment of cardiac disorders, difficult respiration, pneumonia, collapse, asthma, cardiac stricture, new born infant's syncope, narcotic poisoning, injuries, obstruction of blood circulation during injury or surgery, etc.

EXAMPLES OF PRESCRIPTIONS:

1. Aktcor injection fluid 0.7-1.0 cc to be hypodermically injected into the right arm for acute ailments of the heart, difficult respiration, collapse etc.

2. Aktcor fluid 6.0-10.0 cc, Red wine lemonade 200.0 cc. To be taken orally over a two day period for treatment of typhoid fever.

3. Aktcor fluid 0.5-1.0 cc, Hydein fluid 1.5-2.0 cc, Syrup 10.0 cc, Water 50.0 cc. One teaspoonful every three hours for one week in treating children's catarrhal pneumonia.

4. Aktcor fluid 3.0 cc, Solution potassium acetate 3.0-4.0 cc, tincture Gentian 2.0 cc Syrup 6.0 cc, Distilled water 100.0 cc. To be taken three times a day for heart dropsy.

5. Aktcor fluid 4.0-6.0 cc, Infusion Digitalis (0.4-0.6%) 200.0 cc, Syrup 10.0 cc. Three times a day for two days for acute and chronic weakness of the heart.

6. Beuberol fluid 9.0 cc, Aktcor fluid 2.0-3.0 cc, Tincture Nux Vomica 0.5-1.0 cc, Syrup 6.0 cc, Distilled water 100.0 cc. To be taken three times a day for ten days for beriberi leading to cardiac failure.

7. Aktcor fluid 2.0-3.0 cc, Infusion Digitalis (0.3) 100.0 cc, Hydein fluid 3.0 cc, syrup 8.0cc. To be taken three times a day for cardiac weakness in the third stage of pulmonary tuberculosis.

8. Aktcor fluid 3.0-5.0 cc, Infusion Ipecacuanha (0.4%) 160.0 cc, Sodium Iodide 2.0-3.0 gm, Codeine Phosphate 0.1 gm, Syrup 10.0 cc, Water qs 200.0 cc. One spoonful every two hours for influenza.

DIRECTIONS FOR USE AND DOSAGE: Aktcor injection fluid 0.7-1.0 cc can be administered hypodermically several times a day. For children 0.3-0.5 cc according to their age, while 0.5 cc is injected for new born infant's syncope.

Aktcor fluid for oral administration can be taken three times a day, dividing the daily dose of 3 to 5 cc into three doses, before or after meals. Diluted hydrochloric acid may be used with Aktcor for effective medication. Aktcor may be given combined with expectorant cough remedies such as Hydein. It is indicated in pneumonia, bronchitis, stasis catarrh, pulmonary dropsy etc. There were several reports to the effect that satisfactory results were obtained by using Aktcor together with a given quantity of Narcopon injection fluid or Spanidol for coughs and respiratory difficulty in patients suffering from asthma and pulmonary tuberculosis in the final stage.

PACKAGE AND PRICE:

Per-oral liquid; ¥ 1.20 per 25 cc
¥ 3.00 per 100 cc
¥ 11.00 per 500 cc

Ampoules; ¥ 0.80 per 5 ampoules of 1.1 cc each
¥ 1.40 per 10 ampoules of 1.1 cc each
¥ 5.00 per 50 ampoules of 1.1 cc each

MANUFACTURED AND DISTRIBUTED BY:

The Radium Pharmaceutical Company, Inc.
No. 1, 1-chome Kyobashi, Kyobashi-ku, Tokyo.

Factory: 3-chome Takata Minami-cho, Toshima-ku, Tokyo.

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dori, Kyoto.
Fukuoka Branch, Nakajima-machi, Fukuoka.